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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/993,159	11/05/2001	Timothy W. Lovenberg	ORT-1528	8725

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EXAMINER

WILSON, MICHAEL C

ART UNIT PAPER NUMBER

1632

DATE MAILED: 05/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/993,159

Applicant(s)

LOVENBERG ET AL.

Examiner

Michael C. Wilson

Art Unit

1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
 - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
 - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
 - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 2-24-04 (resent 3-1-04).
- 2a) ☒ This action is FINAL. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-7 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-7 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The amendment filed 3-1-04 is a duplicate of the amendment filed 2-24-04.

Applicant's arguments filed therein have been fully considered but they are not persuasive.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-7 remain pending and are under consideration in the instant office action.

The limitation of insensitivity to amnesic effects of scopolamine as demonstrable in a passive avoidance test as new claimed is found on pg 10, lines 10-17.

Claim Rejections - 35 USC § 101

Claims 1-7 remain rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility for reasons of record.

The claims are directed toward a transgenic mouse having a disruption of an endogenous histamine H3 receptor that is insensitive to amnesic effects of scopolamine as demonstrable in a passive avoidance test as compared to a wild-type mouse. The specification teaches H3-/- mice are resistant to the amnesic effect of scopolamine (pg 10, lines 3-25; pg 17, line 21, through pg 18, line 9). The specification does not teach how to use mice that are resistant to the amnesic effect of scopolamine. The art at the time of filing did not teach how to use such a mouse. Since the time of filing, Toyota (2002, Mol. Pharmacol. Vol. 62, pg 389-397, co-written by the inventors) taught H3-/-

mice are resistant to the amnesic effect of scopolamine (pg 396, col. 1, 13-14). However, Toyota does not teach how to use such mice. Toyota concludes the mice should prove important for "elucidating the role of H3 receptors in a variety of peripheral and CNS functions as well as the pathophysiological states that are associated with altered histaminergic activity" (pg 396, col. 2, last sentence). Therefore, while the phenotype of the mouse is specific, the function of H3 receptors in the role of the amnesic effect of scopolamine is not. The insensitivity to scopolamine implies H3 receptors merely play a role in "passive avoidance." It remains unknown how H3 receptors function in the amnesic effect of scopolamine. Overall, the specification does not provide a specific or substantial utility for a mouse that is resistant to the amnesic effect of scopolamine as claimed. Claims 5-6 are included because they are directed toward making the mouse. Claim 7 is included because the cell is isolated from the mouse and because no additional use for the cell alone has been provided.

Applicants argue the mice have utility because they can be used for further research. Applicants point to pg 2, lines 1, 2 and 10-14, pg 4, lines 8-10, pg 7, lines 26-27, and the sentence bridging pg 7-8, which describe using the mice to determine the role of histamine H3 receptor in vivo, to provide a model and evaluate the therapeutic effects of drugs that modulate the function of H3 receptor. Applicants' argument is not persuasive. Further research does not have a specific or substantial utility. Applicants point to Masaki but do not provide any comparisons or teach how mice having a disruption in H1 receptors correlate to mice having a disruption in H3 receptors. The mice do not express H3 receptor; therefore, compounds that modulate the function of

H3 receptor cannot be determined. The mice do not correlate to any disease model. A disruption in a histamine H3 receptor does not correlate to any diseases in humans.

Applicants point to pg 16-18, which teaches testing the mice in passive avoidance tests and sleep-wake states. Applicants' argument is not persuasive. Further research does not have a specific or substantial utility. Drugs that alter the effect of scopolamine in a passive avoidance test can be determined using wild-type mice. The mouse is not a model for any disease state in humans and a disruption in a histamine H3 receptor does not correlate to any disease state in humans. Even since the time of filing, Toyota (2002) has used the mice for further research but has not determined the function of histamine H3 receptor in vivo.

Claim Rejections - 35 USC § 112

Claims 1-7 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for reasons of record.

Claims 1-4 are directed toward a transgenic mouse having a disruption of an endogenous histamine H3 receptor that is insensitive to amnesic effects of scopolamine as demonstrable in a passive avoidance test as compared to a wild-type mouse. The specification teaches H3-/- mice are resistant to the amnesic effect of scopolamine (pg 10, lines 3-25; pg 17, line 21, through pg 18, line 9). The specification does not teach

how to use mice that are resistant to the amnesic effect of scopolamine. The art at the time of filing did not teach how to use such a mouse. Since the time of filing, Toyota (2002, Mol. Pharmacol. Vol. 62, pg 389-397, co-written by the inventors) taught H3-/- mice are resistant to the amnesic effect of scopolamine (pg 396, col. 1, 13-14).

However, Toyota does not teach how to use such mice. Toyota concludes the mice should prove important for "elucidating the role of H3 receptors in a variety of peripheral and CNS functions as well as the pathophysiological states that are associated with altered histaminergic activity" (pg 396, col. 2, last sentence). Therefore, while the phenotype of the mouse is specific, the function of H3 receptors in the role of the amnesic effect of scopolamine is not. The insensitivity to scopolamine implies H3 receptors merely play a role in "passive avoidance." It remains unknown how H3 receptors function in the amnesic effect of scopolamine. The specification merely states the model will allow the "definition of the function of histamine H3 receptor which is critical in deciding the types of modulators are most suitable in therapies" (para. bridging pg 7-8). Overall, the specification does not provide adequate guidance for one of skill in the art at the time of filing to determine how to use a mouse that is resistant to the amnesic effect of scopolamine as a model for any neural disorder or any disease associated with altered histaminergic activity. Even if one of skill used to mouse claimed to screen compounds that altered the "insensitivity to scopolamine" or to "evaluate the therapeutic effects of drugs that modulate the function or expression of histamine H3 receptor equivalents" (pg 2, line 13-15), the specification does not describe how to use mice that are insensitive to the amnesic effect of scopolamine to

evaluate drugs that modulate H3 receptors, how to use compounds obtained from such an evaluation or diseases affected by compounds obtained from such an evaluation. Without teaching the function of H3 receptors or correlating a disruption of H3 receptor to a specific disease, the specification does not enable one of skill to use the mice claimed. Therefore, it would require one of skill undue experimentation to determine how to use the mouse claimed.

The claims encompass any disruption of any histamine H3 receptor gene. The only mouse tested was a mouse homozygous for the disruption (Fig. 1 and 2), which is the only type of disruption that cause the phenotype claimed. Secondly, H3 receptors are a subtype of histamine receptor and encompass at least 2 types (West of record, 1990, Mol. Pharmacol., Vol. 38, pg 610-613). However, the specification does not teach which H3 receptor was disrupted or that a disruption in any H3 receptor causes the phenotype claimed. Therefore, the specification does not provide adequate guidance enabling any disruption in any H3 receptor as broadly claimed causes the phenotype claimed. Applicants have not addressed this rejection.

Claims 5-6 are included because they are directed toward making the mouse. Claim 7 is included because the cell is isolated from the mouse and because no additional use for the cell alone has been provided.

The rejections of claims 2-5 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention have been withdrawn.

The rejection regarding "gene" in claims 2-4 lacking antecedent basis has been withdrawn in view of the amendment to claim 1.

The rejection regarding "a mouse blastocysts" in claim 5, item b) has been withdrawn in view of the amendment to the claim.

The phrase "the blastocyst" in claim 5, item c) lacks antecedent basis.

Conclusion

No claim is allowed.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached on Monday through Friday from 9:00 am to 5:30 pm at (703) 305-0120.

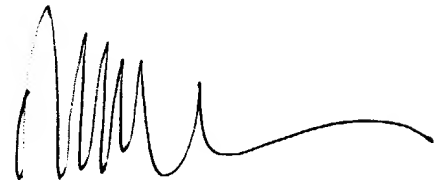
Questions of formal matters can be directed to the patent analyst, Dianiece Jacobs, who can normally be reached on Monday through Friday from 9:00 am to 5:30 pm at (703) 305-3388.

Questions of a general nature relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-1235.

If attempts to reach the examiner, patent analyst or Group receptionist are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051.

The official fax number for this Group is (703) 308-4242.

Michael C. Wilson



MICHAEL WILSON
PRIMARY EXAMINER